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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,436	10/27/2003	Kathleen C.M. Campbell	STU 7397	8942

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	
NOTIFICATION DATE	DELIVERY MODE
05/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/694,436	CAMPBELL, KATHLEEN C.M.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-19 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-19 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/6/2010 has been entered.

Response to Arguments and Amendments

2. Applicant's arguments filed 4/6/2010 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1, 4-20, 23-32 and 38-40 are pending in this office action.

Claim Rejections - 35 USC § 103

5. Claims 1 and 4-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US Patent 6,265,386) as evidence by Pusztai et al. (US Patent 6,110,891) for the reasons made of record in Paper No. 20100120 and as follows.

Applicant argues in general that "The Campbell '386 reference describes methods for reducing hearing or balance loss, damage to ear cell, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and for prolonging survival in patients undergoing treatment with anti-tumor platinum coordination compounds, loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, quinidine, or those exposed to toxic levels of noise or radiation". Applicant further argues that "Pusztai discloses methods for treating mucosal cell damage caused by various agents comprising administration of lectin. Pusztai does not specifically teach treating oral mucosal cell damage apart from any other type oral mucosal cell damage and generally describes nothing more than the state of the art with respect to mucosal cell damage arising from various agents" and "While it is now known that treatment of a patient under chemotherapy with methionine would inherently ameliorate oral mucositis arising from radiation, such inherency was unrecognized in the art, is placed in possession of the art only by the instant application, and thus is not a basis for establishing obviousness under § 103(a)" and therefore not have been an inherent property as argued.

In response Campbell teaches that exposure to radiation, whether intentional as in radiation therapy, can result in gastrointestinal disorders (see col. 18, lines 7-10). Because this is a rejection under 35 USC 103(a), Pusztai was introduced to show that gastrointestinal disorders resulting from the administration of radiation may include the mouth (see col. 6, lines 13-15). Also Pusztai teaches the composition of diets for radiotherapy includes L-methionine (see Table 3, col. 18). Therefore one of ordinary skill in the art would have been motivated to administer L-methionine to reduce oral

mucositis in patients undergoing radiotherapy. The claims broadly recite reducing oral mucositis in a human cancer patient undergoing radiotherapy, and the combination of Campbell and Pusztai makes it obvious to one of ordinary skill in the art to administer L-methionine to reduce oral mucositis in cancer patients undergoing radiation therapy.

Applicant's arguments have been fully considered but they are not persuasive for the reasons given above and that already made of record.

In Summary: Campbell teaches a method of reducing gastrointestinal toxicity, in patients undergoing cancer chemotherapy (i.e., a cancer patient) and undergoing radiation therapy by administering the protective agents D-methionine, L-methionine, a mixture of D and L methionine and a pharmaceutically acceptable salt thereof (see col. 1, lines 12-35, col. 15, lines 25-30 and col. 19, lines 6-8, as required by instant claims 1, 4-6 and 13). Campbell also teaches that the methionine protective agent may be administered orally, and should be given in an amount that will result in a blood serum level equivalent to that achieved parenterally in doses ranging from 1.0 mg-500 mg/kg body weight. See col. 17, lines 44-47, col. 17, lines 30-56 and col. 24, lines 59- 65 (claims 13-17, 29-30). With regards to instant claims 18-19, once the amounts (i.e., 1.0-500 mg/kg body weight) is administered, intrinsically it will maintain a blood serum level of protective agent within the patient of at least 10% or 20-70% of the blood serum level by administration of the effective amount of the protective agent. Campbell also teaches the protective agent is administered from 6 hours before to 6 hours after exposure to chemotherapeutic agent, within 1 hour before and 1 hour after chemotherapeutic agent and one-half hour (30 mins) before and after

chemotherapeutic agent (as required by instant claims 7 and 10-12, see col. 20, lines 8-24). Campbell also teaches that the protective agent may be administered simultaneously and or subsequently with radiation (see col. 19, lines 9-15).

As to the limitation of reducing oral mucositis, Campbell is silent to the specific teaching (i.e., oral mucositis). Nonetheless Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders. As evidence by Pusztai et al. "Mucositis is a painful and debilitating condition in which rapidly growing epithelial cells are damaged and the external mucous layer is removed and/or not replaced sufficiently quickly. Mucositis may result in infection by microorganisms which are present, for example in the mouth or gut. The condition is seen as a major side effect in the treatment of cancer. The incidence and severity of mucositis may increase with increasing rounds of cancer therapy, and may ultimately effect patient treatment compliance and survival", (see col. 1, lines 55-54). Specifically Pusztai teaches that chemotherapeutic agents and radiotherapy are agents that damage the mucosal cells.

Therefore it would have been obvious that Campbell's teachings of treating gastrointestinal symptoms in cancer patients would also reduce oral mucositis in a human or animal cancer patient undergoing chemotherapy because it is well known in the art that cancer patients undergoing chemotherapy and radiation are susceptible to destruction of the mucosal cell in the gut (gastrointestinal) and the mouth as evidence by Pusztai.

6. Claims 1 and 38-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell (US Patent 6,265,386) as evidence by Pusztai et al. (US Patent 6,110,891) for the reasons made of record in Paper No. 20100120 and as follows.

Applicant argues "Claim 38 is dependent on claim 1 and directed to a method of reducing oral mucositis wherein the patient is a cancer patient, is undergoing radiation therapy, and is undergoing treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound. Thus, claims 38-40 are patentable over U.S. Patent No. 6,265,386 (Campbell) in view of U.S. Patent No. 6,110,891 (Pusztai) under 35 U.S.C. § 103(a) for at least the same reasons as claim 1".

In response both Campbell and Pusztai makes it obvious to one of ordinary skill in the art at the time the invention was made because Campbell teaches the patient population includes those who are being administered a platinum containing chemotherapeutic agent (see col. 18, lines 40-45) to patient suffering from variety of cancers which may include cancers that may result in side effects such as oral mucositis in the patient. Further Pusztai teaches that the composition comprising lectin is advantageous in controlling mucosal cell proliferation in patients undergoing chemotherapy and radiotherapy (see col. 8, lines 6-10).

Applicant's arguments have been fully considered but they are not persuasive for the reasons given above and that already made of record.

In summary: Campbell is applied here as above as it relates to claim 1.

Campbell further teaches that the chemotherapeutic effective amount of anti-tumor platinum coordination compound is cisplatin and the protective agent is D-methionine as required by instant claims 38-40, (see abstract).

As to the limitation of reducing oral mucositis, Campbell is silent to the specific teaching (i.e., reducing oral mucositis); nonetheless Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders. As evidence by Pusztai et al. "Mucositis is a painful and debilitating condition in which rapidly growing epithelial cells are damaged and the external mucous layer is removed and/or not replaced sufficiently quickly. Mucositis may result in infection by microorganisms which are present, for example in the mouth or gut. The condition is seen as a major side effect in the treatment of cancer. The incidence and severity of mucositis may increase with increasing rounds of cancer therapy, and may ultimately effect patient treatment compliance and survival", (see col. 1, lines 55-54). Specifically Pusztai teaches that chemotherapeutic agents and radiotherapy are agents that damage the mucosal cells, therefore it would have been obvious that Campbell's method would include reducing oral mucositis in a human or animal cancer patient undergoing chemotherapy because it is well known in the art that cancer patients undergoing chemotherapy and radiation are susceptible to destruction of the mucosal cell in the gut (gastrointestinal) and the mouth, as evidence by Pusztai.

Affidavit

7. The declaration by James Malone under 37 CFR 1.132 filed on 4/6/10 is insufficient to overcome the rejection of claims 1, 4-19 and 38-40 based upon the prior art Campbell (US Patent 6,265,386) and Pusztai et al. (US 6,110,891) as set forth in the last Office action.

Declarant asserts on page 1 para. 2 that "[i]n my review of the literature and experience treating patients, I have found that many patients undergoing radiation therapy do not develop mucositis. For example, radiation treatment is usually targeted to a specific area of the body wherein the diseased tissue is located. Thus, different side effects arise depending on the location of the diseased tissue".

Declarant also asserts that "only portion of the gastrointestinal tract remote from the oral mucosa would result in oral mucositis" and that oral mucosal tissue is very different from the mucosal tissue in other parts of the gastrointestinal tract.

In response the declaration supports Examiners position because Declarant clearly states that "...oral mucositis is sometimes broadly classified as a form of gastrointestinal toxicity...". Campbell teaches that these protective agents (i.e., D/L methionine or mixtures thereof) are employed to ameliorate radiation induced side effects such as gastrointestinal disorders, whether gastrointestinal effect is separate or not Declarant is in agreement with the Examiner that gastrointestinal toxicity is inclusive of oral mucositis which is also supported by Pusztai (see above).

It must be noted that the Declaration by James Malone is an opinion being presented presumably to overcome the rejection of record. The Declaration is made

without underlying facts to support such a position based on sound reasoning that would persuade those skilled in the art. Thus, the Declarant's remarks made in paragraph 2 and 4 are not consistent with the specification. See page 16, lines 14 to the end wherein Applicant being their own lexicographer defines mucositis as "can occur anywhere along the digestive tract from the mouth to the anus" ...and the term mucositis encompasses all forms of mucositis including oral mucositis emphasis added.

Accordingly Ex parte Gelles 22 USPQ 2d 1318 (at 1319) held that "[t]he evidence relied upon also should be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter "as a class" relative to the prior art subject matter." Also in order to show unexpected result's three major points that should be considered: the unexpected result must truly be unexpected, it must be commensurate in scope (show a trend representing the scope), and lastly a direct comparison with the closest prior art of record should be provided.

Declarant's affidavit have been fully considered but found not persuasive for the reasons given.

Double Patenting

8. Claims 1, 4-19 and 38-40 stand rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-9, 11-13,15-25 and 27-33 of U.S. application No. 10/694,432 for the reasons made of record in Paper No. 20100120 and as follows.

Applicant argues that "the '432 application contains claims directed to methods for treating alopecia in a patient experiencing exposure to radiation by administering D-

methionine, L-methionine, or a mixture of D- and L-methionine. Because the mechanism for alopecia and oral mucositis arising from radiation therapy are significantly different, none of the claims of the '432 application provides a reason to try methionine for treatment of oral mucositis in a cancer patient undergoing radiation therapy".

In response contrary to Applicant's assertion that the claims are directed to treating alopecia in a patient experiencing exposure to radiation by administering D-methionine or mixtures thereof, the issue is that the same drug formulation is administered to patients exposed to radiation who are suffering from cancer (as in the instant claims 1, 4-19 and 38-40). Applicant's asserts that the mechanism for treating alopecia and oral mucositis are different. However, there is no mechanistic step recited in the claims other than administering the drug orally, parenterally or topically. Secondly patients undergoing chemotherapy end up losing hair (alopecia) which eventually occurs in patients undergoing radiation therapy.

Thus Applicant's arguments have been fully considered but they are not persuasive for the reason's given above.

9. Claims 1, 4-19 and 38-40 stand rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-29 of (US Patent 7,557,142) and claims 1-36 of (US Patent 6,187,817) for the reasons made of record in Paper No. 20100120 and as follows.

Applicant argues that "...claims 1-28 of the '817 patent are directed to a method for preventing or reducing ototoxicity, claims 29-30 are directed to methods of preventing or reducing weight loss, claims 31-32 are directed to methods of preventing or reducing gastrointestinal toxicity, claims 33-34 are directed to methods of preventing or reducing neurotoxicity, and claims 35-36 are directed to methods of preventing or reducing alopecia" Further Applicant argues that "...because the claims of the '817 patent are not directed to reducing oral mucositis in a cancer patient undergoing radiation therapy, the claims do not include all the elements of subject claims 1 and 3-19".

In response Applicant's argument is found not persuasive because the claims of the patent '142 requires administering L-methionine to patients are receiving chemotherapeutic agent which is also required by the instant application '436 by administering L-methionine. The conditions such as weight loss, reducing gastrointestinal toxicity etc., are all known conditions that occur when a patient is being treated with radiation and or chemotherapeutic agents. Since there is no separate defining step other than solely administering methionine, one of ordinary skill in the art would necessarily expect a reasonable amount of success in reducing these side effects when L-methionine is administered regardless of the patient population.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application is directed to treating diseases (reducing oral mucositis in a patient population undergoing chemotherapy and radiation) and the claims of in the instant claims '142 are directed to reducing the

incidence of ototoxicity in a patient population undergoing chemotherapy with a chemotherapeutic effective amount of an antitumor platinum coordination compound (which is the same as in the instant claims). The claims of the '817 are directed to reducing the ototoxicity in a patient population undergoing chemotherapy with a chemotherapeutic effective amount of an antitumor platinum coordination compound (which is the same as in the instant claims). Since there is no separate defining step other than solely administering methionine for the treatment of conditions related to the use of chemotherapeutic effective amounts of an antitumor platinum coordination compound, because the same population are being treated one of ordinary skill in the art would reasonably expect the different conditions to also be treated in a population experiencing the effects of the same antitumor platinum coordination compound. Radiation is commonly accompanied/combined with treatment of cancers (See evidence by Mori in its entirety).

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. V. G./
Examiner, Art Unit 1618
4/27/10

/Robert C. Hayes/
Primary Examiner, Art Unit 1649